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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,007	01/07/2002	Seiichi P.T. Matsuda	-002376.0990	4712

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/041,007	MATSUDA ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 23-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 23-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/02 and 7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's election of Group I, Claims 1-18 and 23-43 in the reply filed on 8/3/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 19-22 and 44-67 have been cancelled.

Claim 30 is objected to because of the following informalities: the word "encoded" should be "encoding" and the word "containing" should be "contains". Appropriate correction is required.

Applicant is advised that should claims 25, 26, and 30-33 be found allowable, claims 38-43 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 25 and 38 though not identical in wording each recite a unicellular organism comprising an isolated nucleic acid encoding a levopimaradiene synthase. The dependent claims

of each of these are identical and thus 25, 26 and 30-33 are identical to 38-43.

Claim 35 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 is incomplete as depending from cancelled claim 20.

Claims 1, 2, 5-18, and 23-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 5-11, 23, 25, 27-33, 38, and 40-43 are directed to a genus of nucleic acids encoding a levopimaradiene synthase. The specification teaches the structure of only four representative species of such nucleic acids i.e., SEQ ID NOS: 1, 32, 34, and 36 all of which comprise SEQ ID NO:36. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other

than the functionality of encoding a levopimaradiene synthase. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 2, 24, and 34-37 are directed to a genus of nucleic acids comprising SEQ ID NO:38 or encoding SEQ ID NO:39.

The specification does not contain any disclosure of the function of all nucleic acids comprising SEQ ID NO:38 as SEQ ID NO: 39 is a catalytically inactive protein (see page 66, paragraph [224]). The genus of nucleic acids that comprise these above nucleic acids is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated nucleic acids are encompassed within the scope of these claims. The specification discloses only five species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had

possession of the claimed invention at the time the instant application was filed.

Claims 12-18, 26, and 39 are directed to a genus of nucleic acids encoding a levopimaradiene synthase and comprising SEQ ID NO:38 or encoding SEQ ID NO:39. While each of these claims recite a genus of nucleic acids having both structural and functional limitations, the claimed genus is not sufficiently described as the recited structural features are not sufficient to produce a nucleic acid having the recited functional features. The Federal Circuit has said that a sufficient written description of a genus of DNAs may be achieved by a recitation of a representative number of DNAs defined by nucleotide sequence or a recitation of structural features common to members of the genus, which features constitute a substantial potion of the genus. The recited structural feature of the genus (i.e., comprising SEQ ID NO:38) does not constitute a substantial potion of the genus as the remainder of the structure of necessary to encode a polypeptide having levopimaradiene synthase activity is completely undefined. The polypeptide encoded by SEQ ID NO:38 (i.e., SEQ ID NO:39) does not have levopimaradiene synthase activity and the specification does not define the remaining structural features necessary for

members of the genus to be selected. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 2, 5-18, and 23-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids comprising SEQ ID NO:1, SEQ ID NO:32, SEQ ID NO:34, or SEQ ID NO:36 or encoding SEQ ID NO:2, SEQ ID NO:33, SEQ ID NO:35, or SEQ ID NO:37, does not reasonably provide enablement for any nucleic acid encoding a levopimaradiene synthase or any nucleic acid comprising SEQ ID NO:38 or encoding SEQ ID NO:39. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 2, 5-18, and 23-43 are so broad as to encompass any nucleic acid encoding a levopimaradiene synthase or any nucleic acid comprising SEQ ID NO:38 or encoding SEQ ID NO:39.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acids broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleic acid sequence of a single levopimaradiene synthase gene and encoded protein and three active N-terminal truncation variants thereof.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is

unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any nucleic acid encoding a levopimaradiene synthase or any nucleic acid comprising SEQ ID NO:38 or encoding SEQ ID NO:39 because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting levopimaradiene synthase activity; (B) the general tolerance of levopimaradiene synthases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any nucleic acid encoding a levopimaradiene synthase or any nucleic acid comprising SEQ ID

NO:38 or encoding SEQ ID NO:39. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-18, 23-29, 31-35, 38, 39, and 41-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claims 1, 3, 25, 27, 29, and 31 of copending Application No. 10/041,018. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1, 3, 25, 27, 29, and 31 of copending Application No. 10/041,018 and Claims 25, 26, 38, and 39 of the instant application are directed in part to a unicellular organism comprising a nucleic acid sequence encoding the *Ginkgo biloba* levopimaradiene synthase gene of SEQ ID NO:397 (which is identical to SEQ ID NO:1 of the instant application) under the control of a promoter operable in the organism. The claims differ in that the organisms of the copending application further recite that the organism includes one or more additional genes and encompass unicellular organisms comprising a nucleic acid sequence encoding other diterpene synthases besides the *Ginkgo biloba* levopimaradiene synthase gene of SEQ ID NO:397. However, as the *Ginkgo biloba* levopimaradiene synthase gene of SEQ ID NO:397 is disclosed a specific preferred embodiment of the diterpene synthase gene of the claims of the copending application, selection of unicellular organisms including specifically this gene would have been obvious to one of ordinary skill in the art. Alternatively, Claims 25, 26, 38, and 39 of the instant application cannot be considered patentably distinct over Claims

1, 3, 25, 27, 29, and 31 of copending Application No. 10/041,018 when there is a specifically recited embodiment (i.e., unicellular organisms including the *Ginkgo biloba* levopimaradiene synthase gene of SEQ ID NO:397) that would anticipate Claims 25, 26, 38, and 39 of the instant application. As *Saccharomyces cerevisiae, Escherichia coli* and the inducible GAL1 promoter are disclosed as preferred embodiments of the unicellular organism and promoter of the claims of the copending application, selection of *Saccharomyces cerevisiae* or *Escherichia coli* as the unicellular organism and/or the inducible GAL1 promoter as the promoter would have been obvious to one of ordinary skill in the art as well and thus claims 28, 29, 31-33, and 41-43 cannot be considered patentably distinct over Claims 1, 3, 25, 27, 29, and 31 of copending Application No. 10/041,018. Furthermore, the nucleic acids and expression vectors of Claims 1-18, 23-24, 27, 34, and 35 of the instant application would have been obvious from the unicellular organisms of Claims 1, 3, 25, 27, 29, and 31 of copending Application No. 10/041,018 as these are necessary materials for the construction of the organisms of these claims which specifically include the *Ginkgo biloba* levopimaradiene synthase gene of SEQ ID NO:397 of the copending application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Rebecca Prouty
Primary Examiner
Art Unit 1652